REMARKS

Claims 1 and 3-14 are pending in the present application.

At the outset, Applicants wish to thank Examiner Wessendorf for the helpful and courteous discussion with their undersigned Representative on March 26, 2004. During this discussion, several potential amendments and arguments were discussed to address the art of record. The content of this discussion is reflected in the amendment and remarks set forth herein.

Claims 1 and 3-7 provide a method for screening a substance which interacts with a specific region of a biomolecule having an activity, to regulate the activity, said biomolecule being selected from the group consisting of a protein, a nucleic acid and a sugar chain, said method comprising the following steps:

(a) preparing a peptide library composed of a collection of recombinant organisms each presenting at least one of various peptides on its surface;

(b) contacting the recombinant organisms of the peptide library with the biomolecule;

(c) selecting a recombinant organism of the peptide library that interacts with the biomolecule, with a proviso that the interaction is not an antigen-antibody reaction;

(d) testing inhibitory effect of a substance on an interaction between the selected recombinant organism and the biomolecule, wherein said substance is selected from a chemical compound library; and

(e) selecting a substance inhibiting the interaction between the selected recombinant organism and the biomolecule, as the substance which interacts with the specific region of the biomolecule.

Claims 8-14 provide a method for screening a substance which interacts with a specific region of a biomolecule having an activity, to regulate the activity, said biomolecule being selected from the group consisting of a protein, a nucleic acid and a sugar chain, said method comprising the following steps:

(a) a step of constructing a peptide library composed of a collection of recombinant organisms each presenting at least one of various peptides on its surface;

(b) a step of bringing the recombinant organisms of the, peptide library into contact with the biomolecule;

(c) a step of selecting a recombinant organism that interacts with the biomolecule from the peptide library, with a proviso that the interaction is not an antigen-antibody reaction;

(d) a step of determining a peptide presented by the selected recombinant organism and preparing the peptide;

(e) a step of testing inhibitory effect of a substance, on an interaction between the peptide and the biomolecule, wherein said substance is selected from a chemical compound library; and

(f) a step of selecting a substance inhibiting the interaction between the peptide and the biomolecule, as the substance which interacts with the specific region of the biomolecule.

Applicants submit that none of the art of record discloses or suggests either of these methods provided by the present invention. As such, the art of record cannot affect the patentability of the present invention.

The rejections of: (a) Claims 1, 3, and 5-6 under 35 U.S.C. §102(b) over Martens et al, and (b) Claims 1 and 3-7 under 35 U.S.C. §102(b) over O'Neill et al are traversed.

Applicants note that Martens et al and O'Neill et al are silent with respect to steps (d) and (e) in amended Claim 1 and steps (d) – (f) in Claim 8. More specifically, Martens et al and O'Neill et al fail to disclose or suggest a step of testing inhibitory effect of a substance, on an interaction between the selected recombinant organism and the biomolecule, wherein said substance is selected from a chemical compound library; and a step of selecting a substance inhibiting the interaction between the selected recombinant organism and the biomolecule, as the substance which interacts with the specific region of the biomolecule as required by Claim 1. Moreover, Martens et al and O'Neill et al fail to disclose or suggest a step of determining a peptide presented by the selected recombinant organism and preparing the peptide; a step of testing inhibitory effect of a substance, on an interaction between the peptide and the biomolecule, wherein said substance is selected from a chemical compound library; and a step of selecting a substance inhibiting the interaction between the peptide and the biomolecule, as the substance which interacts with the specific region of the biomolecule as required by Claim 8.

The Examiner asserts that the disclosures of Martens et al and O'Neil et al *inherently* anticipate the claimed invention. In particular, the Examiner states that these references disclose inhibitors to the binding of the ligand to the biomolecule as E-selectin and that this disclosure indicates, "such testing would inherently have occurred to afford the inhibitory effect of the inhibitor." (paper number 21, page 8, lines 19-22). Based on this assertion the Examiner apparently concludes that steps (d) and (e) are met.

However, this misguided assertion by the Examiner overlooks the fact that each of these disclosures specifically states that the competitive inhibition assay is performed in a cell-free environment (see Martens et al page 21132, left column, last paragraph and O'Neil et al page 512, left column, second full paragraph). Therefore, contrary to the assertion of the

Examiner, these references ***do not*** disclose or suggest steps (d) and (e), which require the recombinant organism to be present.

Applicants direct the Examiner's attention to MPEP §2112, which states:

> "In relying upon the theory of inherency, the examiner must provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic necessarily flows from the teachings of the applied prior art." *Ex parte Levy*, 17 USPQ2d 1461, 1464 (Bd. Pat. App. & Inter. 1990)

The Examiner has clearly failed to provide any reasonable basis in fact and/or technical reasoning to support a determination of inherency. In fact, all the Examiner has done is simply stated her conclusion, which is contrary to the disclosure of either Martens et al or O'Neil et al.

Not only has the Examiner failed to establish that the present invention is inherently disclosed by Martens et al and/or O'Neil et al, the Examiner is reminded that MPEP § 2141.02 states: "prior art must be considered in its entirety, including disclosures that teach away from the claims". Applicants submit that the disclosure by Martens et al and O'Neil et al that the inhibitory assay is performed in a cell-free environment clearly teaches the artisan away from the claimed invention. When this teaching away is considered, Martens et al and O'Neil et al clearly fail to anticipate and/or render obvious the present invention.

During the discussion with Applicants undersigned Representative the Examiner requested that Applicants specifically indicate where in the specification steps (d) and (e) are disclosed as being performed in the presence of the recombinant organism. To this end, Applicants note that the specification is replete with descriptions supporting the presence of the recombinant organism in steps (d) and (e). For example, descriptions are provided on pages 16-21, as well as in the Examples of the present application (*e.g.*, pages 49-51).

In view of the foregoing, Applicants request withdrawal of the rejections over Martens et al and O'Neil et al.

The rejection of Claims 1 and 3-7 under 35 U.S.C. §112, first paragraph (written description), is traversed.

The Examiner has rejected the claims as lacking sufficient written description for a chemical compound library because the specification "does not describe a chemical compound library, how to make said chemical compound library, the chemical compounds encompassed by said library." (paper number 21, page 6, lines 15-17)

Applicants note that the specification at page 49 clearly states that the candidate inhibitory substance is a "compound in a chemical library." Therefore, the present specification clearly provides explicit support for step (d). The Examiner further asserts that the specification does not describe the chemical compound library, how to make the chemical compound library, or the compounds encompassed in the library (see above). However, the Examiner appears to be overlooking the fact that the specifics of how to make the chemical compound library or the compounds therein are not limiting. The point of the present invention is to screen large chemical compound libraries (e.g., a combinatorial library) by the inventive method to identify *specific* substances that interacts with a specific region of a biomolecule to regulate the activity of the same. Accordingly, the present invention is amenable to any chemical compound library.

Specifically, the present invention provides a general method of identifying lead compounds from a chemical compound library based on the compounds ability to disrupt a preformed interaction between a peptide displayed on the surface of a recombinant organism and a biomolecule binding to the same. Accordingly, the methods of making the chemical compound library or the compounds encompassed in the library are not limiting.

To this end, Applicants **submit herewith** a list of some commercially available chemical compound libraries (Exhibit A) and copies of some selected catalog entries for the same (Exhibit B). Based on these attachments, Applicants note that the skilled artisan would readily appreciate the scope of permissible chemical compound libraries and what the same intends.

Applicants request withdrawal of this ground of rejection.

The rejection of Claims 1 and 3-7 under 35 U.S.C. §112, first paragraph (enablement), is traversed.

As described in the specification at page 6, line 22 to page 7, line 5, the present inventors have determined that screening of a substance interacting with a biomolecule can be efficiently carried out by selecting a substance inhibiting the interaction between the biomolecule and a recombinant organism (or a peptide represented by the recombinant organism) that has been selected from a peptide library composed of a collection of recombinant organisms.

MPEP §2164.01 states:

> The test of enablement is whether one reasonably skilled in the art could make or use the invention from the disclosures in the patent coupled with information known in the art without undue experimentation.

Applicants submit that contrary to the assertions made by the Examiner, with the present specification in hand, the skilled artisan would readily appreciate how to practice the present invention without undue experimentation.

Specifically, Applicants submit that the general steps correlating to steps (a) through (e) in Claim 1 may be performed based on ordinary methods known to the skilled artisan. For

example, Applicants submitted several references with the Amendment and Request for Reconsideration filed September 22, 2003 that showed that the general methods for selection of a recombinant organism that interacts with a biomolecule (generally steps (a) – (c) of Claim 1) would be well within the purview of the skilled artisan. The Examiner points to these references and notes that depending on the components used in these references the conditions are different. In making this assertion it appears that the Examiner is overlooking MPEP §2164.06 and the fact that some experimentation is permissible (e.g., optimization based on the specific components employed). The question that the Examiner should ask is whether that experimentation is undue (MPEP §2164.01).

Based on the foregoing, Applicants submit the specification and the state of the art at the time of the present invention would enable the artisan to practice the full scope of the present invention without undue experimentation. As such, that the presently claimed invention is fully enabled by the specification and the common knowledge available in the art and as such withdrawal of this ground of rejection is requested.

The rejection of Claims 1 and 3-7 under 35 U.S.C. §112, second paragraph, is obviated by amendment.

Applicants have amended Claims 1, 3, and 4 to be free of the criticisms set forth by the Examiner. Specifically, Claim 1 has been amended to remove redundant phrasing and to clarify the "contacting and/or selecting step."

Applicants request withdrawal of this ground of rejection.

Applicants submit that the present application is now in condition for allowance.

Early notification of such action is earnestly solicited.

Respectfully submitted,

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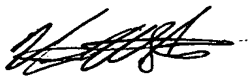

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